

CLAIMS:

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1. An IFNAR2 mutant polypeptide (MIFNAR2) mutated at amino acid residues histidine 78 and asparagine 100, having higher affinity for interferon- β (IFN- β) than the wild type polypeptide, or an analog, functional derivative, fusion protein or salt thereof.
- 10 2. An IFNAR2 mutant polypeptide according to claim 1, wherein the mutations are substitutions.
3. An IFNAR2 mutant polypeptide according to claim 2, wherein the substitutions are non-conservative.
- 15 4. An IFNAR2 mutant polypeptide according to anyone of claims 1 to 3, wherein the histidine residue 78 is substituted by alanine.
5. An IFNAR2 mutant polypeptide according to anyone of claims 1 to 4 wherein the asparagine residue 100 is substituted by alanine, aspartic acid or histidine.
- 20 6. An IFNAR2 mutant polypeptide according to claims 4 and 5, wherein both residues 78 and 100 are substituted by alanine.
7. An IFNAR2 mutant polypeptide according to claim 1 comprising the sequence in SEQ ID NO: 2.
8. An IFNAR2 mutant polypeptide according to claim 1 comprising the sequence in SEQ ID NO: 3.
- 25 9. An IFNAR2 mutant polypeptide according to claim 1 comprising the sequence in SEQ ID NO: 4.
10. An IFNAR2 mutant polypeptide according to anyone of claims 1 to 9, wherein its affinity to IFN- β is about 30 pM.

11. An IFNAR2 mutant polypeptide according to anyone of claims 1 to 9, wherein its affinity to IFN- β is about 25, preferably up to 50 and more preferably up to 100-fold higher than the affinity of the wild type IFNAR2.
12. An IFNAR2 mutant polypeptide according to anyone of claims 1 to 9, wherein the fragment comprises the extracellular domain (MIFNAR2 EC).
13. An IFNAR2 mutant polypeptide according to anyone of claims 1 to 12 being covalently bound to IFN.
14. An IFNAR2 mutant polypeptide according to claim 13, wherein the IFN is IFN- β .
15. An IFNAR2 mutant polypeptide according to anyone of claims 1-14, wherein the IFNAR mutant is PEGylated.
16. A DNA encoding a polypeptide according to anyone of claims 1-14.
17. A DNA according to claim 16, wherein the DNA is fused to a signal peptide sequence.
18. A DNA according to claim 17, wherein the signal peptide sequence is that of the human growth hormone.
19. A vector comprising a DNA according to anyone of claims 16 to 18, capable of expressing the polypeptide encoded by said DNA in a prokaryotic host cell.
20. A vector comprising a DNA according to anyone of claims 16 to 18, capable of expressing the polypeptide encoded by said DNA in a eukaryotic host cell.
21. A prokaryotic host cell comprising the vector according to claim 19.
22. A eukaryotic cell comprising the vector according to claim 20.
23. A method for producing an IFNAR2 mutant polypeptide according to anyone of claims 1 to 14, comprising cultivating a cell according to claim 21 and isolating the IFNAR mutant polypeptide produced.
24. A method for producing an IFNAR2 mutant polypeptide according to anyone of claims 1 to 14, comprising cultivating the cell according to claim 22 and isolating the IFNAR mutant polypeptide produced.

25. The use of the IFNAR2 mutant according to anyone of claims 1 to 15 in the manufacture of a medicament.
26. The use according to claim 25, wherein the medicament further comprises IFN.
- 5 27. The use according to claim 26, wherein the IFN is IFN- β .
28. The use according to claim 25, wherein the medicament further comprises an IFN antagonist.
29. The use according to anyone of claims 25 to 28, for modulating the effects of IFN.
- 10 30. The use according to claim 29, for enhancing the activities of IFN.
31. The use according to claim 30, for enhancing the anti-cancer activities of IFN.
32. The use according to claim 30, for enhancing the immune modulatory therapeutic properties of IFN.
- 15 33. The use according to claim 30, for enhancing the immune modulatory activities of IFN in autoimmune diseases selected from multiple sclerosis, rheumatoid arthritis, myasthenia gravis, diabetes, lupus and ulcerative colitis.
34. The use according to claim 28 or 29, for inhibiting the activity of IFN.
- 20 35. A pharmaceutical composition comprising a therapeutically effective amount of the IFNAR2 mutant according to anyone of claims 1 to 15.
36. A pharmaceutical composition comprising a gene therapy expression vector, expressing a therapeutically effective amount of the IFNAR2 mutant according to anyone of claims 1 to 15.
- 25 37. A pharmaceutical composition according to claim 35 or 36, further comprising IFN.
38. A pharmaceutical composition according to claim 37, wherein the IFN is IFN- β .

39. A pharmaceutical composition according to claim 35 or 36, further comprising an IFN antagonist.
40. A pharmaceutical composition according to claim 38, wherein the IFNAR2 mutant and IFN- β are covalently bound.
- 5 41. A pharmaceutical composition according to claims 35 and 40, wherein the fragment of IFNAR2 mutant comprises the extracellular domain.
42. A pharmaceutical composition according to anyone of claims 35 to 41, for augmenting the anti-viral properties of IFN.
- 10 43. A pharmaceutical composition according to claim 42, for the treatment of chronic granulomatous disease, condyloma acuminatum, juvenile laryngeal papillomatosis, hepatitis A or chronic infection with hepatitis B and C viruses.
44. A pharmaceutical composition according to anyone of claims 35 to 41, for augmenting the anti-cancer properties of IFN.
- 15 45. A pharmaceutical composition according to claim 44, for the treatment of hairy cell leukemia, Kaposi's sarcoma, multiple myeloma, chronic myelogenous leukemia, non-Hodgkins's lymphoma or melanoma.
46. A pharmaceutical composition according to anyone of claims 35 to 41, for augmenting the immune modulating properties of IFN.
- 20 47. A pharmaceutical composition according to claim 46, for treatment of diseases selected from multiple sclerosis, rheumatoid arthritis, myasthenia gravis, diabetes, ulcerative colitis and lupus.
48. A pharmaceutical composition according to claim 39, for the inhibition of immune modulating properties of IFN.
- 25 49. A method of treatment of an autoimmune disease comprising administration of a therapeutically effective amount of an IFNAR2 mutant polypeptide according to anyone of claims 1 to 15.
50. A method according to claim 49, wherein the autoimmune disease is selected from multiple sclerosis, rheumatoid arthritis, myasthenia gravis, diabetes, lupus and ulcerative colitis.
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51. A method of treatment of a viral disease comprising administration of a therapeutically effective amount of an IFNAR2 mutant polypeptide according to anyone of claims 1 to 15.
52. A method of treatment according to claim 51, for the treatment of chronic granulomatous disease, condyloma acuminatum, juvenile laryngeal papillomatosis, hepatitis A or chronic infection with hepatitis B and C viruses.
53. A method of treatment of cancer comprising administration of a therapeutically effective amount of an IFNAR2 mutant polypeptide according to anyone of claims 1 to 15.
54. A method according to claim 53, for the treatment of hairy cell leukemia, Kaposi's sarcoma, multiple myeloma, chronic myelogenous leukemia, non-Hodgkins's lymphoma or melanoma.
55. A method of treatment according to anyone of claims 49 to 54, further comprising a therapeutically effective amount of IFN- β
56. A method of treatment of a disease caused or aggravated by IFN- β comprising the inhibition of immune modulating properties of IFN by administration of an IFNAR2 mutant polypeptide according to anyone of claims 1-15.
57. A method of treatment according to claim 56, further comprising the administration of an IFN- β antagonist.
58. The use of the IFNAR2 mutant polypeptide according to anyone of claims 1 to 14 in a formulation to prevent IFN oligomerization.
59. The use according to claim 58, to prevent IFN- β oligomerization.
60. An IFN formulation comprising the IFNAR2 mutant polypeptide according to anyone of claims 1 to 14.
61. A formulation according to claim 60, wherein the formulation comprises IFN- β .